A new diagnostic platform for prediction of
drug response based on a tumor’s microRNA profile

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Introduction
Increasing evidence suggests that microRNAs play a role in the initiation and progression of cancer, and therefore, may comprise a novel class of molecular biomarkers with prognostic and predictive potential. For example, microRNAs that are differentially expressed in tumor tissue compared to normal tissue can be used as diagnostic biomarkers for the detection of cancer. However, a major impediment to the successful development of therapeutic treatment of cancer is the current inability to predict which patients are likely to benefit from specific chemotherapy drugs. Current tests rely on the ex vivo growth of a tumor in the presence of chemotherapeutic drugs but new molecular tools are needed. We have developed a novel colon cancer screening test that has been preliminarily tested in the Extreme Drug Resistance assay, a clinically validated drug resistance test (Figure 1). Each sample is microfluidized and placed on a miRCURY LNA™ microRNA Array, which allows for very sensitive and specific detection of small RNA targets like microRNAs.

Methods
Samples
Two formalin-fixed, paraffin-embedded (FFPE) sections from patient (median age: 63.3 y, range: 25.9-91.2 y) diagnosed with colon cancer were analyzed. Three full rows were used per chemotherapy:

- EDR-Irinotecan (Ir)
- EDR-5FU
- EDR-Oxaliplatin (Ox)

The samples were characterized with respect to resistance status, i.e. low (LDR), intermediate (IDR) or extreme (EDR) drug resistance towards a panel of chemotherapeutic drugs, including 5-FU, Oxaliplatin, Irinotecan, and DNAplatin.

Results – Technology
Figure 5

*Figure 5: The miRCURY LNA™ microRNA Array enables the rapid and nonradioactive detection of microRNA expression profiles in FFPE tissue samples.

Figure 6

*Figure 6: The miRCURY LNA™ microRNA Array enables the detection of microRNA expression profiles in FFPE tissue samples.

Results – miRNAs

Table 1

<table>
<thead>
<tr>
<th>miRNA</th>
<th>T-test (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-155</td>
<td>0.01</td>
</tr>
<tr>
<td>miR-210</td>
<td>0.001</td>
</tr>
<tr>
<td>miR-221</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Figure 7

Figure 8

Figure 9

Figure 10

Conclusion
It is possible to determine the EDR status of colorectal cancer based on the tumor's miRNA profile.

We are currently validating the classifier in an independent test set.